

CLAIMS

1. An antibody or an antigen binding fragment thereof having the CDR-H3 sequence selected from the group consisting of: SEQ ID NO: 27, SEQ ID NO: 28, SEQ ID NO: 5 29, SEQ ID NO: 30, and SEQ ID NO: 31.

2. An antibody or an antigen binding fragment thereof having the CDR-L3 sequence selected from the group consisting of: SEQ ID NO: 32, SEQ ID NO: 33, and SEQ ID NO: 34.

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3. An antibody or an antigen binding fragment thereof having a CDR-H3 sequence selected from the group consisting of: SEQ ID NO: 27, SEQ ID NO: 28, SEQ ID NO: 29, SEQ ID NO: 30, and SEQ ID NO: 31, and a CDR-L3 sequence selected from the group consisting of: SEQ ID NO: 32, SEQ ID NO: 33, and SEQ ID NO: 34.

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4. A method for identifying candidate sequences of at least the CDR3 region of antibodies specific against at least one antigen produced by *Clostridium difficile* during an infection or against a vaccine, comprising the steps of:

- (i) with B cells isolated from at least one patient who has been infected by *Clostridium difficile* or administered said vaccine, sequencing at least the CDR3 region of the VH and/or VL coding regions of said B cells; and
- (ii) correlating said sequenced at least the CDR3 regions of the VH and/or VL coding regions of said B cells from said at least one patient to identify a set of candidate sequences for at least a CDR3 region of antibodies specific against said at least one antigen produced by *Clostridium difficile* or against said vaccine, each of said set of candidate CDR3 sequences or a sequence having at least 80% homology therewith occurring in total at a frequency of 20 25 at least 1 percent in the set of sequences determined at step (i).

5. A method according to claim 4, said B cells being selected from the group consisting of peripheral B-cell lymphocytes and B cells from the spleen.
6. A method according to claim 5, said peripheral B-cell lymphocytes being isolated
5 from blood from said at least one patient.
7. A method according to any of claims 4-6, said at least one antigen being an immunogen.
- 10 8. A method according to any of claims 4-7, said at least one patient displaying a pronounced antibody response in response to infection by *Clostridium difficile*.
9. A method according to any of claims 4-8, said at least one patient having recovered
15 from infection by *Clostridium difficile*.
10. A method according to any of claims 4-9, said correlation step (ii) comprising determining putative amino acid sequences from said sequenced at least the VH and/or VL CDR3 coding regions, and correlating said putative amino acid sequences.
- 20 11. A method according to claim 9, said correlation step (ii) comprising identifying the Complementarity Determining Regions comprised in said at least the VH and/or VL regions and correlating said Complementarity Determining Regions.
- 25 12. A method according to claim 11, said Complementarity Determining Regions being selected from the group consisting of CDR1, CDR2 and CDR3.
13. A method according to any of claims 4-12, said correlation step (ii) additionally correlating at least one of the group consisting of: the strain of *Clostridium difficile*

infecting said at least one patient, the time point at which said B cells are isolated during infection of said at least one patient by *Clostridium difficile*, the age of said at least one patient, the sex of said at least one patient, and the race of said at least one patient.

5 14. A method according to any of claims 4-13, said B cells having been isolated from said at least one patient at a plurality of time points during infection of said at least one patient by *Clostridium difficile*, said correlation step (ii) correlating the time point during infection of said at least one patient by *Clostridium difficile* at which said B cells are isolated.

10 15. A method according to any of claims 4-13, said B cells having been isolated from at least two patients, at least one of whom has recovered from infection by *Clostridium difficile*, and at least one of whom has not recovered from infection by *Clostridium difficile*, said correlation step (ii) correlating the recovery of said at least two patients from 15 infection by *Clostridium difficile*.

16. A method according to any of claims 4-13, said B cells having been isolated from at least two patients, said patients being infected by different strains of *Clostridium difficile* producing said at least one antigen, said correlation step (ii) correlating said sequenced at 20 least the VH and/or VL coding regions of said B cells to identify a set of candidate sequences for antibodies, each of which is specific against at least one shared antigen produced by said different strains of *Clostridium difficile* or is specific against different antigens produced by said different strains of *Clostridium difficile*.

25 17. A method of manufacture of a medicament for the treatment of an infection by *Clostridium difficile* which produces at least one antigen, comprising the steps of:
(i) performing a method according to any of claims 4-16; and

(ii) synthesising at least one antibody comprising at least one candidate sequence specific against said at least one antigen produced by *Clostridium difficile*.

18. A method of manufacture of a medicament according to claim 17, comprising the 5 step of combining said synthesised at least one antibody with a pharmaceutically acceptable carrier, diluent or excipient.

19. A method of treatment of an infection of a patient by *Clostridium difficile* which produces at least one antigen, comprising the steps of:

10 (i) performing a method according to any of claims 4-16;
(ii) synthesising at least one antibody comprising at least one candidate sequence specific against said at least one antigen produced by *Clostridium difficile*; and
15 (iii) administering a therapeutically effective quantity of said at least one synthesised antibody to said patient.

20. A method of producing a database which identifies candidate sequences for antibodies specific against at least one antigen produced by *Clostridium difficile*, comprising the steps of:

20 (i) performing a method according to any of claims 4-16; and
(ii) storing the data produced by said method in said database.

21. A method of generating a report which identifies candidate sequences for antibodies specific against at least one antigen produced by *Clostridium difficile*, comprising the steps 25 of:
of:

(i) performing a method according to any of claims 4-16; and
(ii) producing a report comprising the data produced by said method.

22. A method for determining the efficacy of a vaccine, comprising the steps of:

- (i) with B cells isolated from at least one patient who has been administered said vaccine, sequencing at least the CDR3 region of the VH and/or VL coding regions of said B cells; and
- 5 (ii) correlating said sequenced at least the CDR3 region of the VH and/or VL coding regions of said B cells to identify a set of candidate sequences for at least the CDR3 region of antibodies specific against said vaccine, each of said set of CDR3 candidate sequences or a sequence having at least 80% homology therewith occurring in total at a frequency of at least 1 percent in the set of sequences determined at step (i).

10 23. A method according to claim 22, correlation step (ii) comprising correlating said sequenced at least a CDR3 region of the VH and/or VL coding regions of said B cells with sequenced at least a CDR3 region of the VH and/or VL coding regions of B cells isolated from at least one patient who has been infected with *Clostridium difficile* against which vaccination with said vaccine is intended to stimulate a protective immune response.

15 24. A method according to either of claims 22 or 23, said correlation step (ii) additionally correlating at least one of the group consisting of: the time since administration of said vaccine to said at least one patient, the age of said at least one patient, the sex of said at least one patient, the race of said at least one patient, and the Complementarity Determining Regions of said sequenced at least the VH and/or VL coding regions.

20 25. A method according to any of claims 22-24, said method determining the efficacy of said vaccine in stimulating a protective immune response against *Clostridium difficile* against which vaccination with said vaccine is intended to stimulate a protective immune response.

26. A method of producing a database which identifies the efficacy of a vaccine, comprising the steps of:

- (i) performing a method according to any one of claims 22-25; and
- (ii) storing the data produced by said method in said database.

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27. A method of generating a report which identifies the efficacy of a vaccine, comprising the steps of:

- (i) performing a method according to any one of claims 22-25; and
- (ii) producing a report comprising the data produced by said method.

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28. A diagnostic test method for identifying a *Clostridium difficile* infection in a patient, comprising the steps of:

- (i) with B cells isolated from said patient, sequencing at least the CDR3 region of the VH and/or VL coding regions of said B cells;
- (ii) comparing said sequenced at least said CDR3 region of the VH and/or VL coding regions of said B cells with a set of sequences for at least the CDR3 region of antibodies specific against *Clostridium difficile*, and determining whether each of said set of CDR3 sequences or a sequence having at least 80% homology therewith occurs in total at a frequency of at least 1 percent in the set of sequences determined at step (i); and
- (iii) correlating the results of comparison step (ii) to determine the presence or absence of a *Clostridium difficile* infection in said patient.

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29. A diagnostic test method for determining the susceptibility of a patient to *Clostridium difficile* infection, comprising the steps of:

- (i) with B cells isolated from said patient, sequencing at least the CDR3 region of the VH and/or VL coding regions of said B cells;

5 (ii) comparing said sequenced at least said CDR3 region of the VH and/or VL coding regions of said B cells with a set of sequences for at least the CDR3 region of antibodies specific against *Clostridium difficile*, and determining whether each of said set of CDR3 sequences or a sequence having at least 80% homology therewith occurs in total at a frequency of at least 1 percent in the set of sequences determined at step (i); and

(iii) correlating the results of comparison step (ii) to determine the susceptibility of said patient to *Clostridium difficile* infection.

10 30. A diagnostic test kit for performing a diagnostic test method according to any one of claims 28-29.